



THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Detlef P. Muller-Schulte  
Serial No: 10/516,629 / Conf. No. 4567  
Filed: December 1, 2004  
Title: THERMOSENSITIVE POLYMER CARRIER WITH CHANGEABLE PHYSICAL STRUCTURE FOR BIOCHEMICAL ANALYSIS, DIAGNOSTICS AND THERAPY  
Examiner / Group Art Unit: \_\_\_ / Art Unit 1616  
Attorney File: RO0940US (#90568)

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-4150

SUBMISSION OF NOTIFICATION OF THE RECORDING OF A CHANGE

Sir:

Enclosed for addition to the file of the above-identified application is a copy of the "Notification of the Recording of a Change" dated 30 November 2004 which confirms that the inventor, Detlef P. Muller-Schulte, is the applicant for the application in the United States.

Respectfully submitted,

By: \_\_\_\_\_

D. Peter Hochberg  
Reg. No. 24,603

DPH/SM/ck  
Enc.

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Certificate of Mailing

I hereby certify that this document, and anything indicated as being attached or enclosed, is being deposited with the United States Postal Service as First Class mail in an envelope addressed: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-4150, on the date noted below:

Christine Kotran: Christine Kotran

Date: 5/27 / 2005

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

FLACCUS, Rolf-Dieter  
Bussardweg 10  
50389 Wesseling  
Germany

Date of mailing (day/month/year) 30 November 2004 (30.11.2004)			
Applicant's or agent's file reference MS 001/2003 PCT	<b>IMPORTANT NOTIFICATION</b>		
International application No. PCT/EP2003/005614	International filing date (day/month/year) 28 May 2003 (28.05.2003)		

1. The following indications appeared on record concerning:				
<input checked="" type="checkbox"/> the applicant	<input checked="" type="checkbox"/> the inventor	<input type="checkbox"/> the agent	<input type="checkbox"/> the common representative	
Name and Address MÜLLER-SCHULTE, Detlef, P. Martelenberger Weg 8 52066 Aachen Germany		State of Nationality DE		State of Residence DE
		Telephone No.		
		Facsimile No.		
		Teleprinter No.		

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:				
<input checked="" type="checkbox"/> the person	<input type="checkbox"/> the name	<input type="checkbox"/> the address	<input type="checkbox"/> the nationality	<input type="checkbox"/> the residence
Name and Address MAGNAMEDECS GMBH Martelenberger Weg 8 52066 Aachen Germany		State of Nationality DE		State of Residence DE
		Telephone No.		
		Facsimile No.		
		Teleprinter No.		

3. Further observations, if necessary: <b>Applicant in Box 1 has transferred his rights to the person in Box 2 who is sole applicant only for all designated States except US. Applicant 1 remains on record as applicant for US only and inventor for all designated States. Corr. of IB/306 issued 17.11.2004.</b>				
4. A copy of this notification has been sent to:				
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned			
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned			
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:			

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Antonia MULLER (Fax : 338 89 75)
Facsimile No. (41-22) 338.89.75	Telephone No. (41-22) 338 8243

006522673



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Attorney File: RO0940US (#90568)

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-4150

SUBMISSION OF ENGLISH TRANSLATION OF IPER

Sir:

As the above-identified application is the U.S. national phase of PCT/EP2003/005614, we are enclosing copies of the English translation of the International Preliminary Examination Report having a completion date of 10 September 2004 and of its Notification of Transmittal of Copies of Translation to the elected Offices with a mailing date of 27 January 2005.

Respectfully submitted,

By: \_\_\_\_\_

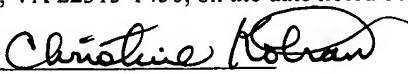
  
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Certificate of Mailing

I hereby certify that this document, and anything indicated as being attached or enclosed, is being deposited with the United States Postal Service as First Class mail in an envelope addressed: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date noted below:

Christine Kotran:   
Date: 5 / 27 / 2005

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 72.2)

To:

FLACCUS, Rolf-Dieter  
Bussardweg 10  
50389 Wesseling  
ALLEMAGNE

**Eingegangen**

- 2. FEB. 2005

FRIST:.....

Date of mailing (day/month/year) 27 January 2005 (27.01.2005)
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Applicant's or agent's file reference MS 001/2003 PCT
--

**IMPORTANT NOTIFICATION**

International application No. PCT/EP2003/005614
--

International filing date (day/month/year)  
28 May 2003 (28.05.2003)

Applicant MÜLLER-SCHULTE, Detlef, P. et al
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**1. Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

**2. Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

CA, CN, CO, KR, RU

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AU, BR, BY, EA, EP, ID, IL, IN, IS, JP, MX, NO, NZ, PH, PL, SG, TR, US, ZA

**3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

**It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.**

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer

Ellen Moyse

Facsimile No.+41 22 740 14 35

Facsimile No.+41 22 338 89 75



Translation

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MS 001/2003 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/005614	International filing date (day/month/year) 28 May 2003 (28.05.2003)	Priority date (day/month/year) 01 June 2002 (01.06.2002)
International Patent Classification (IPC) or national classification and IPC A61K 41/00		
Applicant MÜLLER-SCHULTE, Detlef, P.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 7 sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 24 December 2003 (24.12.2003)	Date of completion of this report 10 September 2004 (10.09.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/005614

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

 the international application as originally filed the description:

pages \_\_\_\_\_, 1-35, as originally filed

pages \_\_\_\_\_, filed with the demand

pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

 the claims:

pages \_\_\_\_\_, 5-21, 22 (in part), as originally filed

pages \_\_\_\_\_, as amended (together with any statement under Article 19

pages \_\_\_\_\_, filed with the demand

pages \_\_\_\_\_, 22(in part),23-39,40(in part) // 1-4,40(in part),41-45, filed with the letter of 06.03.2004 // 30.08.2004

 the drawings:

pages \_\_\_\_\_, as originally filed

pages \_\_\_\_\_, filed with the demand

pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

 the sequence listing part of the description:

pages \_\_\_\_\_, as originally filed

pages \_\_\_\_\_, filed with the demand

pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

 the language of a translation furnished for the purposes of international search (under Rule 23.1(b)). the language of publication of the international application (under Rule 48.3(b)). the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

 contained in the international application in written form. filed together with the international application in computer readable form. furnished subsequently to this Authority in written form. furnished subsequently to this Authority in computer readable form. The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.4.  The amendments have resulted in the cancellation of: the description, pages \_\_\_\_\_ the claims, Nos. \_\_\_\_\_ the drawings, sheets/fig \_\_\_\_\_5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/005614

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.  
 claims Nos. 1-45 (in part)

because:

- the said international application, or the said claims Nos. 45 relate to the following subject matter which does not require an international preliminary examination (*specify*):

See the Supplemental Box.

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

- the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.  
 no international search report has been established for said claims Nos. 1-45 (in part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- the written form has not been furnished or does not comply with the standard.  
 the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/05614

**Supplemental Box**  
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III

1. An international search report was established only for the products indicated in the embodiments. Accordingly, the international preliminary examination report has been established only with respect to the subject matter for which a search has been carried out.
2. Claim 45 relates to subject matter that, in the opinion of the Examining Authority, comes under PCT Rule 67.1 (iv). Therefore, no written opinion has been established with respect to the industrial applicability of the subject matter of said claim (PCT Article 34(4)(a)(i)).

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP 03/05614

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	1-45	YES
	Claims		NO
Inventive step (IS)	Claims	1-45	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-44	YES
	Claims		NO

## 2. Citations and explanations

3. This report makes reference to the following documents:

- D1: APPLIED MICROBIOLOGY AND BIOTECHNOLOGY 41,  
1994, 99-105.
- D2: JOURNAL OF FERMENTATION AND BIOENGINEERING  
84 (4), 1997, 337-341.
- D3: BIOTECHNOLOGY PROGRESS., 17, No. 2, March 2001  
(2001-03), 369-375
- D4: JOURNAL OF BIOMATERIALS SCIENCE, 11, No. 2,  
2000, 123-147
- D5: WO 01/05586 A
- D6: WO 03/026618 A.

3.1 D1 discloses magnetic, thermosensitive polymers made of poly(styrene/N-isopropylacrylamide/methacrylic acid) latex particles containing magnetite. A structural change takes place owing to heating. Said document describes the use of said polymers for antibody purification. The production takes place in a two-stage process. D2 discloses polymers of this type, a temperature-dependent change in their structure, and their use for enzyme immobilization. Said document does not describe inverse dispersion

during production. D3 likewise discloses thermosensitive polymers containing N-isopropylacrylamide to which magnetite particles are added during polymerization and which show a temperature-dependent change in structure. The magnetism is used for faster sedimentation. The production takes place in a two-stage process.

- 3.2 D4 discloses thermosensitive polymers (poly(N-isopropylacrylamide/methacrylic acid)), their pH- and temperature-dependent structural changes, and their potential use as active substance carriers.
- 3.3 D5 discloses thermosensitive polymers (poly(N-isopropylacrylamide/methacrylic acid hydrogels)) containing metals (gold) which, when heated by means of electromagnetic radiation, lead to a structural change in the polymers, whereby active substances are released. Two-layer systems are described, and their use as microparticles is proposed (page 14).
- 3.4 D6 discloses thermosensitive particles (for example, made of thermosensitive polymers) treated with ultrasound in order to release active substances. Assuming a valid priority date, said document is not considered to be prior art for the purposes of the international preliminary examination.
4. The subject matter of claims 1-45 appears to be novel.
- 4.1 Claim 1 relates to thermosensitive polymers containing magnetic and/or metal colloids and characterized in that they can be produced by inverse suspension polymerization and in that their

physical structure can be changed by magnetic induction. D1-D3 and D5 disclose thermosensitive polymers that contain magnetic or metallic particles but are not produced by inverse suspension polymerization. Since, according to the applicant (see pages 13 and 14), the suspension polymerization influences the quality of the polymer articles, the subject matter of claims 1-24 appears to be novel.

- 4.2 Claims 25 and 26 relate to a method for producing thermosensitive polymers. Since none of documents D1-D5 discloses such a method, the subject matter of said claims appears to be novel.
- 4.3 Claim 43 relates to a method for releasing active substances by means of alternating magnetic fields, and claim 44 relates to a method for modifying the physical structure. Since none of documents D1-D5 discloses such a method, the subject matter of said claims appears to be novel.
- 4.4 Accordingly, claim 45, which relates to the use of these polymers in extremely different fields with the involvement of an alternating magnetic field, likewise appears to be novel.
5. Since none of documents D1-D5 discloses or renders obvious the use of alternating magnetic fields for releasing, the subject matter of claims 43 and 44 appears to be inventive. For the same reason, the subject matter of claims 1-42 and 45 appears to be inventive.